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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/042,583	03/17/1998	JIAN NI	PF366	5224

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EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/042,583	NI, ET AL.	
	Examiner	Art Unit	
	Claire M Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *287-322,324,326-432,434-442,446-491,507-517,553-596,598-608,611-619 and 622-632* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 287-322,324,326-432,434-442,446-491,507-517,553-596,598-608,611-619 and 622-632.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 2, 4004, has been entered.

Response to Amendment

The rejection of claims under 35 USC 102(e) and 103 as anticipated by or obvious over US Patent 6,072,047 is withdrawn in view of Applicants' arguments that the patent does not receive priority to parent application 08/815,255, filed 3/12/97. This and the earlier priority application have an insufficient disclosure of the DR5 encoding nucleic acid or protein such that the patent could receive benefit of priority for the instantly claimed subject matter.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Pending claims are rejected under the judicially created doctrine of double patenting over claims 1-48 of U. S. Patent No. 6,743,625 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: the specie claims of the patent render the genus claims of the instant application obvious because the subject matter is overlaps.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 553-564 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence at least 90% identical to amino acids 1-133 of SEQ ID NO:2, wherein said polypeptide induces apoptosis or binds TRAIL, does not reasonably provide enablement for an isolated polynucleotide encoding polypeptide comprising an amino acid sequence at least 90% identical to amino acids 1-113 of SEQ ID NO:2, wherein said polypeptide binds an antibody with specificity for the polypeptide consisting of amino acids 1-360 of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

While being enabled for a polynucleotide encoding a polypeptide with a sequence at least 90% identical to SEQ ID NO:2 or the extracellular domain thereof, which polypeptide induces apoptosis or binds TRAIL, the specification is not enabling for those polypeptides which bind an antibody with specificity for SEQ ID NO:2 but do not induce apoptosis or bind TRAIL. There

are a very large number of polypeptides, not to mention polynucleotides as claimed, which meet the structural requirements of the claim but share no function with SEQ ID NO:2 or the encoding polynucleotide, respectively. The specification has not taught how to use such polypeptides or polynucleotides. The sharing of an antibody binding site does not confer enablement to a polypeptide. While the skilled artisan could use an *antibody* that binds SEQ ID NO:2, it would require undue experimentation to us a polypeptide bound by the antibody if that polypeptide did not share the property of inducing apoptosis or binding to TRAIL as disclosed for SEQ ID NO:2.

Claims 362-373 and 404-415 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide consisting of the recited amino acid fragment with recited identity to the corresponding fragment of SEQ ID NO:2 , does not reasonably provide enablement for a polynucleotide comprising the fragment with recited identity to the corresponding fragment of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims..

The claims are drawn to a polynucleotide comprising a nucleic acid encoding a polypeptide comprising a sequence at least 90% identical to a fragment, wherein the sequence has a function; however, the claimed polynucleotide, encoding nucleic acid or polypeptide does not need to have a function. The functional limitation recited in the claims limits the amino acid sequence to at least 90% identical to a designated fragment of SEQ ID NO:2 instead of limiting the encoded polypeptide. The fragment of claim 362 is the intracellular domain (ICD), and claim 404 is the death domain (DD). Even if an ICD or DD were part of another polypeptide, the polypeptide may or may not retain any functionality imparted by the domain when it is part of the protein it naturally occurs in, except perhaps antigenicity. For claims in which the domain is not identical to the disclosed domain sequence of DR5, it is unpredictable how this domain would function out of context even if it were able to function within a "DR5 variant" recited in the claims. While several DD-containing proteins were known in the prior art, mix-and-match domains for the proteins are not shown, and which amino acids can be changed so that the

domain will impart a function within a heterologous sequence is not disclosed. The specification provides no working examples of polypeptides comprising only one of the domains recited in the claims. How and if a domain would function within a polypeptide would be dependent on the sequence of the polypeptide and positioning of the domain sequence within the polypeptide. The specification does not provide guidance for the skilled artisan to be able to use a commensurate number of encoding polynucleotides as recited without undue experimentation commensurate with the scope of the claims.

Claims 507-517, 608, 611-619 and 622 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide of at least 50 contiguous amino acids of the designated region of SEQ ID NO:2, does not reasonably provide enablement for a polynucleotide encoding a polypeptide comprising the at least 50 contiguous amino acids, wherein the polypeptide has no function or is bound by an antibody with specificity for amino acids 1-360 of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a polynucleotide comprising a nucleic acid which encodes a polypeptide, but for claim 507, the functional limitation recited in the claim limits the 50 amino acid fragment comprised by the polypeptide instead of the recited polypeptide or encoding nucleic acid. For claim 608, there is no functional limitation. The specification does not provide guidance or working examples to allow the skilled artisan to use a polypeptide comprising the fragment even if the polypeptide comprises a binding site for an antibody that binds SEQ ID NO:2. Binding of a polypeptide by an antibody does not alone provide enablement. It would require undue experimentation to use the claimed polypeptide.

Claims 553-564 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated polynucleotide comprising a nucleic acid encoding a polypeptide comprising an amino acid sequence having at least 90% or 95% sequence identity with a particular disclosed sequence, which polypeptide binds an antibody with specificity for the polypeptide of amino acids 1-360 of SEQ ID NO:2. The claims are to polynucleotides comprising a nucleic acid encoding a genus of polypeptides, only a small number of which have been described. For example, the portion of the polypeptide comprising the region with the specified identity to SEQ ID NO:2 is not necessarily the portion which is bound by the antibody. Such polypeptide have not been described. Further, because the claims use the open language of a "polypeptide comprising", the claims are structurally very broad and include polypeptides in which the recited activity is not due to the amino acid sequence at least 90% identical to amino acids 1-133 pr 1-360 of SEQ ID NO:2. Those polynucleotides which are described are those encoding polypeptides meeting the structural requirements which also induce apoptosis or bind TRAIL or those consisting of the recited amino acid sequence. The portion of the genus which has not been described is that encoding a polypeptide which meets the structural requirements of the claim but shares no active function with SEQ ID NO:2 as well as the portion encoding a polypeptide in which the region outside the specified amino acid sequence is the region conferring the recited function.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. There is not identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Which encoded polypeptides of the genus comprising the required sequence are part of the invention has not been set forth.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in

possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only those polynucleotides encoding polypeptides meeting the structural requirements and which also induce apoptosis or bind TRAIL or those consisting of the recited amino acid sequence, but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claims 362-373 and 404-415 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a polynucleotide comprising a nucleic acid encoding a polypeptide comprising an amino acid sequence having at least 90% or 95% sequence identity

with a particular disclosed sequence in which the functional limitation in the claims is directed to the amino acid sequence instead of the encoded polypeptide. The claims do not require that the polypeptide itself possess any particular biological activity or conserved structure. The claims are drawn to a genus of polynucleotides encoding polypeptides which are defined only by sequence identity and only a small subset of which have been described. Because the claims use the open language of a "polypeptide comprising", the claims are structurally very broad. There are a very large number of polypeptides which meet the structural requirements of the claim but share no active function with SEQ ID NO:2.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not identification of a particular portion or of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Which polypeptides of the genus comprising the required sequence are part of the invention has not been set forth.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotides encoding polypeptides comprising the particular recited fragments which are identical to the specified fragment of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Conclusion

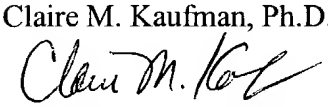
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

August 5, 2004